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**IN THE UNITED STATES PATENT AND TRADEMARK OFFICE**
**BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES**

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| Applicant(s): | Jack A. Maggiore et al. | ) | |
| Application No. | 10/074,715 | ) | |
| Filed: | February 13, 2002 | ) | Group Art Unit: 1641 |
| For: | BIOLOGICAL FLUID STABILIZING COMPOSITION AND METHOD OF USE THEREOF | ) | |
| Examiner: | Gailene R. Gabel | ) | Attorney Docket No. BMT-107 |

**BRIEF ON APPEAL**

Mail Stop Appeal Brief - Patents
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

This is an appeal from the final rejection of claims 12-18, 20-22, and 32 in the above-identified application. This revised Appeal Brief is being presented in response to the Notification of Non-Compliant Appeal Brief mailed on March 7, 2006. No additional fee is due.

**1. Real Party in Interest.**

This application is assigned to BioSafe Medical Technologies, Inc.

**2. Related Appeals and Interferences.**

There are no related appeals or interferences.

**3. Status of All Claims.**

Claims 12-18, 20-22, and 32 are rejected. Claims 1-11, 19, 23-31, 33, and 34 have been cancelled. The claims are presented in Appendix A hereto. Claim 12 is an independent claim. The rejection of claims 12-18, 20-22, and 32 is being appealed.

**4. Status of All Amendments Filed Subsequent to Final Rejection.**

A response to the final Office Action was filed and entered. Rejections of claims 12-18, 20-22, and 32 under 35 U.S.C. §112 were withdrawn in an advisory action

dated September 22, 2005. Rejection of claims 12-18, 20-22, and 32 under 35 U.S.C. §103(a) was maintained. No claims were amended subsequent to the final rejection.

**5. Summary of the Claimed Subject Matter.**

The present invention provides an aqueous biological fluid preserving composition suitable for lysing and preserving a blood sample for hormone analysis. The composition is capable of preserving thyroid stimulating hormone present in the blood sample for at least about three weeks at an ambient temperature of about 22 °C (page 7, lines 3-6 and 22-28, page 11, line 13 through p. 13, line 8) and consists essentially of about 0.05 to about 0.5 weight percent of a chelating agent (page 4, lines 24-25), about 5 to about 25 weight percent of a cell lysing agent (page 4, line 24), up to about 0.1 weight percent of a preservative (page 4, line 25), up to about 50 weight percent of an antifreeze agent (page 4, lines 28-29); and the remainder being water (page 4, line 26).

Claims 13-18, 20-22, and 32 each depend either directly or indirectly from claim 12, and incorporate all of the limitations thereof.

Claim 13 specifies that the chelating agent is a calcium chelating agent (original claim 13 and page 5, line 23).

Claim 14 specifies that the chelating agent is EDTA (original claim 14 and page 5, line 19).

Claim 15 specifies that the cell lysing agent is a $C_1$-$C_4$ alcohol (original claim 15 and page 5, lines 1-2).

Claim 16 specifies that the cell lysing agent is ethanol (original claim 16 and page 5, lines 3-4).

Claim 17 specifies that the preservative is present in an amount of about 0.01 to 0.03 wt % (original claim 17 and page 4, lines 26-27).

Claim 18 specifies that the preservative is sodium azide (original claim 18 and page 6, lines 15-16).

Claim 20 specifies that the antifreeze agent is an organic polyol (original claim 20 and page 4, lines 26-27), while claim 21 specifies that the organic polyol is a $C_1$ to $C_{10}$ polyol (original claim 21 and page 6, lines 19-20), and claim 22 specifies that the organic polyol is ethylene glycol (original claim 22 and page 6, line 21).

Claim 32 is directed to an article of manufacture comprising the biological fluid

preserving composition of claim 12 in packaged form (original claim 32 and page 8, lines 6-16).

**6. Grounds of Rejection to be Reviewed on Appeal.**

Claims 12-18, 20-22, and 32 stand rejected under 35 U.S.C. §103(a) as being obvious over U.S. Patent No. 6,579,688 (Steaffens *et al.*) in view of U.S. Patent No. 5,616,460 (Figard).

**7. Argument.**

**I. Claims 12-18, 20-22, and 32 Are Not Obvious Over U.S. Patent No. 6,579,688 (Steaffens *et al.*) in view of U.S. Patent No. 5,616,460 (Figard).**

Claims 12-18, 20-22, and 32 stand rejected under 35 U.S.C. §103(a) as being unpatentable over U.S. Patent No. 6,579,688 (Steaffens *et al.*) in view of U.S. Patent No. 5,616,460 (Figard). This rejection is clearly unwarranted. A *prima facie* case for obviousness requires that the references themselves must contain some teaching, suggestion, or motivation to combine their teachings. *In re Bell,* 26 USPQ2d 1529, 1531 (Fed. Cir. 1993); *In re Fine*, 5 USPQ2d 1596, 1598 (Fed, Cir. 1988). Moreover, an obviousness analysis requires that the prior art both suggest the claimed subject matter and reveal a reasonable expectation of success to due reasonably skilled in the art. *In re Vaeck*, 20 USPQ2d 1438, 1442 (Fed. Cir. 1991). Neither prong of this analysis has been satisfied in this instance. Furthermore, a *prima facie* case for obviousness requires that all claim limitations be taught or suggested by the prior art. *In re Royka*, 180 USPQ 580 (CCPA 1974). All words in a claim must be considered in judging the patentability of that claim against the prior art. *In re Wilson*, 165 USPQ at 496. The instant rejection falls short of these requirements.

Steaffens *et al.* is directed to a reagent for stabilizing polypeptides and antigens used in analytical procedures. The entire focus of Steaffens *et al.* is on compositions that contain a serum protein (e.g., bovine serum albumin or fetal calf serum) and a detergent as key, active ingredients. As noted in the Amendment dated August 2, 2005 (the "After-Final Response"), the final Office Action cites col. 3, lines 55-64 from the summary of the invention as support for the rejection. This cited passage is merely a generic list of components that *could* be present in the stabilizing composition and would have provided no guidance to one of ordinary skill in the art, whatsoever:

"In certain preferred embodiments, the reagent comprises one or more of the following: buffer(s), blocking agent(s), solvent(s), salt(s), chelator(s), detergents(s), and preservative(s)."

Similarly, the cited section at col. 4, line 33 to col. 5, line 6 simply defines each of the components recited at col. 3, lines 55-64. In contrast to these general descriptions, however, the specific teaching of Steaffens *et al.* is that a serum protein compound and a detergent are important, as active ingredients, to achieve suitable preservation of antigens and polypeptides. The purported improved preserving compositions in Steaffens *et al.* are described in the detailed description, beginning at col. 8, line 30. From this passage, one of ordinary skill in the art would have understood that the compositions described as being part of the purported invention of Steaffens *et al.* include, *inter alia*, a serum protein, such as fetal calf serum (FCS) or bovine serum albumin (BSA), as well as a detergent. All of the claims also require the presence of a serum and a detergent in the compositions.

The reference teaches, at col. 9, lines 15-30, the importance and significance of the serum material and of the detergent as active participants in the purported preserving activity of the compositions. For example, the reference indicates that fetal calf serum may include "other stabilizing materials" (col. 9, line 20), and that the detergent may maintain important secondary structures and supportive associations of the antigen or polypeptide, while disrupting unimportant or degradative structures or interations (see col. 9, lines 27-30). It is clear from these passages that Steaffens *et al.* teach that the serum protein compound and detergent are both key ingredients of the preservative compositions.

Frigard teaches an entirely different type of composition than Steaffens *et al.*, i.e., a buffer composition containing dithiothreitol (DTT) and ethylene glycol as the active buffering components (see, e.g., the abstract, as well as the description at col. 2, line 40 through col. 3, line 2; col. 3, lines 15-21, and col. 4, line 33-67). The purpose of the DTT is described as preventing oxidation of sulfhydryl groups in a protein (see col. 4, lines 33-52), while the purpose of the ethylene glycol is described as preventing oxidation of the DTT (see col. 4, lines 53-67).

Each of claims 12-18, 20-22, and 32 includes all of the limitations of claim 12, which is directed to a composition suitable for lysing and preserving a blood sample for hormone analysis. The composition of claim 12 *consists essentially of* specified amounts of a

chelating agent, a cell lysing agent, a preservative, and an antifreeze agent, in water. Furthermore, the composition is capable of preserving thyroid stimulating hormone (TSH) present in a blood sample for at least about 3 weeks at an ambient temperature of about 22 °C. As presently defined, the claims exclude other active ingredients, due to the relatively closed "consisting essentially of" language of the claims.

The applied references merely contain isolated, *general* disclosures of the various classes of compounds specified by the claims. Notably, the references do not teach or suggest the combined specific amounts of chelating agent, cell lysing agent, preservative or antifreeze agent set forth in the present claims. The references themselves do not contain any motivation for one of ordinary skill in the art to have combined the isolated teachings of the references to obtain the *specific compositions* of the present claims. The fact that the Examiner has done so is evidence of impermissible hindsight reconstruction of the claimed invention using Applicants' own specification as a guide.

As noted in the After-Final Response, the specific teachings Steaffens *et al.* actually teach away from the presently claimed invention. The cited references specifically teach the importance of serum protein materials and detergents (Steaffens *et al.*) for preserving antigens and polypeptides. The present claims exclude such materials. Furthermore, the combined references do not teach or even suggest a composition that is capable of preserving thyroid stimulating hormone (TSH) in a blood sample for at least about 3 weeks at an ambient temperature of about 22 °C. Certainly there is no teaching or suggestion that would have provided one of ordinary skill in the art with a reasonable expectation of success at preserving TSH in a blood sample for at least about 3 weeks, since, as noted previously, the references are silent with respect to TSH stability.

In response to the arguments previously presented by Applicants, the Office Action states, on page 10, that the preservation capability limitation of the claims does not set out a structural limitation for the claimed compositions. This statement misses the point that the structural limitations of the claims are set forth in the lettered elements "a" through "d" in claim 12. However, the structural limitations of the claims must still be read in light of the TSH stability requirement. All words in a claim must be considered in judging the patentability of that claim against the prior art. *In re Wilson*, 165 USPQ at 496.

Certainly, one of ordinary skill in the art would not have had a reasonable expectation of success in achieving the requisite TSH stability by combining the components set forth in the present claims based on the combined teachings of the references, assuming, *arguendo*, that these references are combinable. The applied references are silent with regard to TSH preservation and require components (i.e., a serum protein and a detergent) not present in the claimed compositions. The is no teaching or suggestion in the applied art to omit the serum protein and detergent from the compositions of Steaffens *et al.* in any event.

The Advisory Action dated September 22, 2005, purports to respond to arguments made by Applicants in the After-Final Amendment. The Advisory Action completely ignores the presence of a detergent component in the Steaffens *et al.* compositions. The "consisting essentially of" transitional phrase of claim 12 excludes both the serum protein and the detergent components taught by Steaffens *et al.* In addition, the Advisory Action asserts that the serum protein materials of the Steaffens *et al.* compositions are present only as a "protein diluent" (see page 4, last paragraph). This assertion is without any basis in the applied references and appears to represent the Examiner's own, unsupported opinion. The Advisory Action does not address Applicants' position regarding the detergent component at all.

The characterization on page 4 of the Advisory Action that the composition of Steaffens *et al.* "consists essentially of" EDTA as chelating agent and a cell lysing or dispersing agent such as ethanol evidences an impermissible hindsight-evaluation of the reference in light of the teachings of the present application. This characterization ignores the clear teaching in Steaffens *et al.* that a *serum protein and a detergent* are required.

The presence of a serum protein in the compositions of Steaffens *et al.* also raises potential storage stability issues for the compositions themselves, even in the absence of a biological fluid sample, since serum proteins can potentially degrade and support microbial growth during storage, prior to use. The present compositions avoid this potential storage stability (or shelf-life) issue, since a protein component is not present in the composition prior to adding a biological fluid sample for analysis.

The Advisory Action states, on page 7, that the TSH preserving activity of the claimed compositions "does not render the product novel". The present claims have been rejected on the basis of obviousness, not lack of novelty, however. Accordingly, all of the

advantages of the claimed compositions should be considered as factors in assessing patentability. The TSH preserving activity and the lack of a protein component are two such advantages not disclosed in or even suggested by the applied art.

**II. Conclusion**

A *prima facie* case for obviousness has not been established. Claims 12-18, 20-22, and 32 are clearly patentable over the applied art. The rejection of these claims should be reversed.

Respectfully submitted,

Dated: 22 March 2006

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## APPENDIX A

## CLAIMS ON APPEAL

Claim 12. An aqueous biological fluid preserving composition suitable for lysing and preserving a blood sample for hormone analysis, the composition consisting essentially of:

a) about 0.05 to about 0.5 weight percent of a chelating agent;

b) about 5 to about 25 weight percent of a cell lysing agent;

c) up to about 0.1 weight percent of a preservative;

d) up to about 50 weight percent of an antifreeze agent; and

e) the remainder being water;

the composition being capable of preserving thyroid stimulating hormone present in the blood sample for at least about three weeks at an ambient temperature of about 22 °C.

Claim 13. The composition of claim 12 wherein the chelating agent is a calcium chelating agent.

Claim 14. The composition of claim 12 wherein the chelating agent is ethylenediaminetetraacetic acid (EDTA) or a salt thereof.

Claim 15. The composition of claim 12 wherein the cell lysing agent is a $C_1$ - $C_4$ alcohol.

Claim 16. The composition of claim 15 wherein the cell lysing agent is ethanol.

Claim 17. The composition of claim 12 wherein the preservative is present in an amount in the range of about 0.01 to about 0.03 weight percent.

Claim 18. The composition of claim 17 wherein the preservative is sodium azide.

Claim 20. The composition of claim 12 wherein the antifreeze agent is an organic polyol.

Claim 21. The composition of claim 20 wherein the organic polyol is a $C_1$ - $C_{10}$ polyol.

Claim 22. The composition of claim12 wherein the antifreeze agent is ethylene glycol.

Claim 32 An article of manufacture comprising an aqueous biological fluid preserving composition of claim 12 in packaged form.

| Notification of Non-Compliant Appeal Brief (37 CFR 41.37) | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/074,715 | MAGGIORE ET AL. | |
| | Examiner | Art Unit | |
| | Gailene R. Gabel | 1641 | |



*--The MAILING DATE of this communication appears on the cover sheet with the correspondence address--*

The Appeal Brief filed on *16 December 2005* is defective for failure to comply with one or more provisions of 37 CFR 41.37.

To avoid dismissal of the appeal, applicant must file anamended brief or other appropriate correction (see MPEP 1205.03) within **ONE MONTH or THIRTY DAYS** from the mailing date of this Notification, whichever is longer. **EXTENSIONS OF THIS TIME PERIOD MAY BE GRANTED UNDER 37 CFR 1.136.**

1. ☐ The brief does not contain the items required under 37 CFR 41.37(c), or the items are not under the proper heading or in the proper order.

2. ☒ The brief does not contain a statement of the status of all claims, (e.g., rejected, allowed, withdrawn, objected to, canceled), or does not identify the appealed claims (37 CFR 41.37(c)(1)(iii)).

3. ☐ At least one amendment has been filed subsequent to the final rejection, and the brief does not contain a statement of the status of each such amendment (37 CFR 41.37(c)(1)(iv)).

4. ☐ (a) The brief does not contain a concise explanation of the subject matter defined in each of the independent claims involved in the appeal, referring to the specification by page and line number and to the drawings, if any, by reference characters; and/or (b) the brief fails to: (1) identify, for each independent claim involved in the appeal and for each dependent claim argued separately, every means plus function and step plus function under 35 U.S.C. 112, sixth paragraph, and/or (2) set forth the structure, material, or acts described in the specification as corresponding to each claimed function with reference to the specification by page and line number, and to the drawings, if any, by reference characters (37 CFR 41.37(c)(1)(v)).

5. ☐ The brief does not contain a concise statement of each ground of rejection presented for review (37 CFR 41.37(c)(1)(vi))

6. ☐ The brief does not present an argument under a separate heading for each ground of rejection on appeal (37 CFR 41.37(c)(1)(vii)).

7. ☐ The brief does not contain a correct copy of the appealed claims as an appendix thereto (37 CFR 41.37(c)(1)(viii)).

8. ☐ The brief does not contain copies of the evidence submitted under 37 CFR 1.130, 1.131, or 1.132 or of any other evidence entered by the examiner **and relied upon by appellant in the appeal**, along with a statement setting forth where in the record that evidence was entered by the examiner, as an appendix thereto (37 CFR 41.37(c)(1)(ix)).

9. ☐ The brief does not contain copies of the decisions rendered by a court or the Board in the proceeding identified in the Related Appeals and Interferences section of the brief as an appendix thereto (37 CFR 41.37(c)(1)(x)).

10. ☒ Other (including any explanation in support of the above items):

*Appellant identified and provided incorrect set of finally rejected claims in page 1 of the Brief on Appeal.*

Gailene R. Gabel
Patent Examiner
Art Unit 1641